



## **Biocompatibility of Nitinol Stapes Prosthesis**

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**Abstract:** **OBJECTIVE:** Use of the SMart piston, a nitinol-based, self-crimping prosthesis in stapes surgery may allow improved functional results because of better sound transmission properties at the incus-prosthesis interface because of the elimination of manual crimping. Possible disadvantages include thermal damage or strangulation of the incus and its mucoperiosteum or nickel intolerance. The goal of this study was to morphologically assess the fixation of this prosthesis to the incus, investigate the reaction of the middle ear mucosa to the prosthesis, identify alterations to the incudal bone, and detect deposits of nickel in the tissue around the prosthesis. **STUDY DESIGN::** Prospective consecutive case analysis. **SETTING::** Tertiary referral center. **PATIENTS:** Four patients with an unfavorable functional result after primary SMart-piston stapedotomy. **INTERVENTION:** Revision malleostapedotomy with explantation of the incus and prosthesis for further analysis. **MAIN OUTCOME MEASURES:** Analysis of intraoperative findings and postoperative examination of the explants using light- and scanning-electron microscopy, energy dispersive x-ray analysis, and atom absorption spectrometry. **RESULTS::** The intraoperative, macroscopic, and scanning electron microscopic investigation showed tight circular fixation of the prostheses, whereas a gap between the prosthesis and the lateral incus was found in 1 case. All prostheses were overgrown by mucosa. Superficial localized erosion of the incudal bone was found in 2 cases. There was no elevation in nickel content in the removed tissue samples. **CONCLUSION::** The lateral gap between prosthesis and incus did not affect fixation of the prosthesis, neither did covering by a mucosal layer. Bone erosion was most likely caused by laser in one and by the prosthesis in another explant. No signs of increased nickel deposits could be found on energy dispersive x-ray analysis or atom absorption spectrometry. We conclude that a nitinol stapes prosthesis is safe for treatment of stapedia fixation.

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# Biocompatibility of Nitinol Stapes Prosthesis

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## **Abstract**

**Objective:** Use of the SMart piston, a nitinol-based, self-crimping prosthesis in stapes surgery may allow improved functional results because of better sound transmission properties at the incus-prosthesis interface due to the elimination of manual crimping. Possible disadvantages include thermal damage or strangulation of the incus and its mucoperiosteum or nickel intolerance. The goal of this study was to (1) morphologically assess the fixation of this prosthesis to the incus, (2) investigate the reaction of the middle ear mucosa to the prosthesis, (3) identify alterations to the incudal bone, (4) detect deposits of nickel in the tissue around the prosthesis.

**Study design:** Prospective consecutive case analysis

**Setting:** Tertiary referral center.

**Patients:** Four patients with an unfavorable functional result after primary SMart-piston stapedotomy.

**Intervention:** Revision malleo-stapedotomy with explantation of the incus and prosthesis for further analysis.

**Main outcome Measures:** Analysis of intraoperative findings and postoperative examination of the explants using light- and scanning-electron microscopy, energy dispersive x-ray analysis (EDAX) and atom absorption spectrometry.

**Results:** The intraoperative, macroscopic and scanning electron microscopic investigation showed tight circular fixation of the prostheses, while a gap between the prosthesis and the lateral incus was found in one case. All prostheses were overgrown by mucosa. Superficial localized erosion of the incudal bone was found in two cases. There was no elevation in nickel content in the removed tissue samples.

**Conclusion:** The lateral gap between prosthesis and incus did not affect fixation of the prosthesis neither did covering by a mucosal layer. Bone erosion was most likely caused by laser in one and by the prosthesis in another explant. No signs of increased nickel deposits could be found on EDAX or atom absorption spectrometry. We conclude that a nitinol stapes prosthesis is safe for treatment of stapedial fixation.

## **Introduction**

Since the introduction of stapedotomy as standard treatment for otosclerosis by Shea (1) in 1958, not only has the surgical technique improved but also a variety of different prostheses have been developed. Nevertheless, fixation of the prosthesis on the long process of the incus remains one of the most difficult and critical steps in the surgical procedure. Optimal crimping has a major influence on the postoperative hearing results, but there are surgical risks for middle and inner ear damage (2). In order to overcome these difficulties, a thermo- activated prosthesis composed of a nitinol-based hook and a Teflon-based piston was introduced by Gyrus-ENT (Berlett, TN, USA). Nitinol is a metal alloy of nickel (45%) and titanium (55%) that was developed by Buehler et al. in 1962 (3). More sophisticated nitinol products have been developed over time with the advent of less invasive surgical procedures (4). Nitinol is used for stents or catheters in several disciplines such as gastroenterology, pneumology, cardiology and urology (5), and as a stapes prosthesis in Otology (6). This alloy has a specific characteristic in that after heating it above an activation temperature of between 40 and 50°C, its shape changes to a predefined form due to shape-memory conformation(6). Non-touch heat-activated fixation reduces the risk of trauma to the ossicular chain, specifically its joints, and to the inner ear by minimizing manipulation of the ossicles and the prosthesis within the vestibule. It allows a snug fit between the prosthesis and the incus and avoids the technically challenging manual crimping. Studies show comparable (7-10) or better sound transmission properties of heat-activated nitinol prostheses and conventional prosthesis (11, 12). The clinical safety and efficacy of its use has been reported in several studies (e.g., 7-8). However, there are also limitations to the prosthesis. It is possible that the pressure of the prosthesis on the long process of the incus may lead to erosion of the bone.

Nitinol may induce an inflammatory reaction of the mucosa in the middle ear (13). Mucosal growth may improve stabilization of the prosthesis on the incus. However, scar tissue may also grow between the prosthesis and the incus, thereby dampening sound transmission.

A circular fixation of the prosthesis on the incus may lead to strangulation of its blood supply. This in turn could result in necrosis of the lenticular process, although the main blood supply is provided through the body of the incus. The heat application necessary for crimping may also damage the bone and the mucoperiosteum. Furthermore, nickel may potentially cause a toxic or allergic reaction as up to 16 % of the population suffers from an allergy to nickel (14, 15). There have been no reported experimental results concerning the toxic reactions of middle ear structures to nickel and the role of nickel as an allergen in the middle ear. Only one report of sensorineural hearing loss and development of grey exudation in the middle ear after stapedotomy using a nitinol prosthesis exists. However it remains unclear if a straightforward relationship existed between nickel and the reported tissue reaction (13).

The goal of this study was to investigate the properties of a nitinol-based prosthesis (SMart-Piston [Gyrus-ENT, Berlett, TN USA]) after implantation by (1) morphologically assessing the fixation of the prosthesis to the incus, (2) investigating the reaction of the middle ear mucosa to the prosthesis, (3) identifying alterations to the incudal bone and (4) detecting deposits of nickel in the tissue around the prosthesis.

## **Material and Methods**

From a cohort of 120 consecutive patients that underwent stapedotomy for otosclerosis between January 1<sup>st</sup>, 2004, through December 31<sup>st</sup>, 2008 using a SMart-Piston (Gyrus-ENT, Berlett, USA), four patients needed revision due to unfavorable hearing results after 6 to 40 months (mean 22 months). These patients (2 men and 2 woman) between 41 and 62 years of age are labeled as A, B, C, and D as shown in table 1. The initial stapedotomy in these four patients was performed between June 1<sup>st</sup> 2005 and June 1<sup>st</sup> 2007 in 1 right and 3 left ears (table 1). For stapes revision surgery, routinely malleo-stapedotomy is performed, as more favorable results are achieved compared to revision stapedotomy in our hands (16). The study was approved by our internal review board and performed according to the principles of Helsinki. Informed consent was obtained for all four patients to having the removed prosthesis and incus analyzed for this investigation. During revision surgery, fixation of the prosthesis on the incus and mobility of the malleus were assessed with a fine hook, while position of the prosthesis in the oval window, adhesions in the middle ear and mobility of the malleus and incus were documented. An intraoperative Laser Doppler Interferometry (LDI) was used to assess the vibrations of the long process of the incus and the prosthesis loop as described elsewhere (12, 17). The frequency range of 0.25 to 5 kHz was tested. The long process of the incus was carefully cut with a hand held optical fiber laser (Ceralas G5 532nm, 5W; CeramOptec GmbH, Germany) and removed together with the attached prosthesis. This was possible in three cases, but in one case the prosthesis had to be detached from the lenticular process to allow safe removal without danger of damage to the chorda tympani. Despite the tight fixation of prosthesis on, it could be detached without significant dislocation of the long incus process. This was done by introducing a the tip of a 1.5 mm hook between the prosthesis and the incudal bone and carefully lifting the prosthesis by turning the hook while continuously inspecting the motions of the incus. The removed specimens were stored in formalin and analyzed. An examination of the prosthesis was performed macroscopically (Leica Z16 APO, Leica-Microsystems GmbH, Germany) to document fixation of the prosthesis on the long process of the incus.

A precise representation of the surface was achieved by scanning electron microscopy (SEM) (FESEM SUPRA 50 VP, Carl Zeiss, Germany). The extent of mucosal overgrowth over the prosthesis was checked, and the existence and size of bony erosion of the incus was recorded. For SEM, the explants were fixed in a 2.5% glutaraldehyde buffered solution before they were dehydrated in alcohol with increasing concentrations (10, 25, 50, 75, 50 and 100% ethanol). Afterwards, they were transferred into a critical-point-dryer, which was used to replace water within the explants first by ethanol and then by liquid CO<sub>2</sub> (18).

After SEM, the prosthesis was carefully removed from the incus . After another carbon evaporation deposition, the amount of nickel was checked by energy dispersive x-ray analysis (19) using an SEM (FESEM SUPRA 50 VP, Carl Zeiss, Germany) with an integrated EDX-detector (EDAX Detecting Unit PV7715/89ME, Ametek GmbH, Germany). Two areas from posterior portion the former attachment of the prosthesis to the incus were determined on each explant for investigation. Next, the explants were metal sprayed with platinum (SCD 500 Sputter Coater, BAL-TEC AG, Liechtenstein) and again analyzed by SEM in order to evaluate bone erosions. Normal cortical bone is expected to be smooth while an erosion exposes the trabecular bone of the incus core.

Finally atom absorption spectrometry (GTA 120 Graphit Tube Atomizer, Varian, USA) was performed to determine the content of nickel on the long process of the incus.

The incus were aggregated in 200µl nitric acid, dissolved in a thermo mixer (Thermomixer comfort, Eppendorf, Germany) at 90°C and 1500rpm and then centrifuged for 10 minutes at 16000g (Centrifuge 5416R, Eppendorf, Germany) before analysis. The results were compared to a positive (25ppb-nickel-standard-solution), and a negative (nitric acid) control and to four incuses that had not been in contact with a prosthesis. These four incuses served as a control and were removed during autopsy. Three measurements for each specimen were averaged. Detection threshold of atom absorption spectrometry is in the µg/l to ng/l (ppb-ppt) range.

## **Results**

Intraoperative examination showed firm fixation of all four prostheses that could be confirmed by manual palpation and LDI. Sound transmission loss measured by LDI was below 3 dB at the measured frequency range. One prosthesis (Explant D) was fixed in the oval window niche by scar tissue while the perforation was at the correct location in the central or inferior-central third of the footplate (20). The top of this prosthesis was overgrown and firmly fixed to the bone by scar tissue, whereas all other prostheses were positioned as expected in the oval window niche. Adhesions of the middle ear mucosa in the mesotympanum were documented in Explant A and D. Restricted mobility of the malleus was seen in Explant A and D (Table 2). The mobility of the ossicular chain was normal in patient B and C, but the tympanic membrane was thickened due to scar tissue. The reason for conductive hearing loss remained unclear in patient C. It did only partially improve after revision.

Macroscopic examination of the explants (Table 3) confirmed a circular and firm fixation of two of them (A and C). Explant D had anterior and posterior contact of the incus and the prosthesis. Additionally, the prosthesis did not completely attach to the incus in the lateral part, and a gap between the bone and the prosthesis was visible (figure 1).

Two series of SEM were performed. The fixation of the prosthesis on the incus and the extension of mucosa over the prosthesis were evaluated in the first series. The bony erosions of the incus were investigated in the second series. Because the prosthesis was removed intraoperatively for Explant B, fixation of the prosthesis could only be checked in Explants A, C and D. Macroscopically, a circular tight attachment of the incus was visible in Explants A and C, and a lateral gap between the bone and prosthesis was present in Explant D. There was firm contact in the anterior and posterior part in Explant D (figure 2). The loop of the prosthesis was completely overgrown by mucosa in all three explants (figure 2). Even the piston was covered by mucosa in Explants A and D. There was no correlation between amount of mucosa and time interval between stapedotomy and revision. In Explant C, the incus was covered by mucosa, and at the location where the prosthesis was removed intraoperatively, a disruption of mucosa was visible, suggestive of an overgrowth of the prosthesis loop with mucosa. An area of superficial bony erosion with clear edges was found in Explants B and C. There was no circularly or on both sides eroded bone in any of the explants (Figure 3). The round, bowl like loss of cortex with exposed bone trabeculae is visible in the posterior part of the incus of Explant C. It measures 0.5 mm in diameter and has a depth of 0.2 mm at the center. In Explant B, superficial longish-oval erosion was found in the anterior part. Its diameter measured approximately 0.3 mm. There was no evidence of carbonized bone in any of the explants, and no erosion was found in Explants A and D.

The quantitative evaluation of the content of nickel on the surface of the incus using energy dispersive x-ray analysis was negative. Therefore, the amount of nickel found

on the surface of the incus of each explant was below the limit of detection. Iron and aluminum were detected additionally to the elements representing the normal constitution of bone (phosphorous, calcium, oxygen, carbon, nitrogen and sodium). Atom absorption spectrometry of the bone showed a content of nickel between 2.15 and 3.99 µg/g (Table 4). These values are in the range of the values from the four controls, which was between 1.86 and 4.04 µg/g thus below the normal nickel concentrations in human tissues (21).

## **Discussion**

Regardless the surgical technique or the material of the prosthesis used, some patient develop a new conductive hearing loss after stapedotomy and require revision surgery. A revision was necessary in 3.3 % (4/120) of our patients. The cause of failures of the primary surgery can only be investigated and evaluated during revision surgery and are shown in table 2. These findings correspond to the results of Lesinski et al. (22), who showed in a series of 279 consecutive stapedotomy revisions that the most common cause for failure is prosthesis migration out of the oval window fenestration due to development of scar tissue. Other possible reasons include a fixed or loose prosthesis, a subluxated, fixed or eroded malleus or incus, and fibrosis or regrowth of otosclerotic bone in the oval window (23).

### **Prosthesis fixation**

Intraoperatively, there was a tight fixation of all 4 prostheses on the incus. These findings were confirmed by macroscopy and SEM (available for Explant A, C, and D) in Explant A and C while a gap in the lateral part between the bone and the prosthesis hook was visible in Explant D. The exact position of the lateral part of the prosthesis is sometimes not well visible because of the view of the surgeon from lateral on the prosthesis. This is the reason why the lateral gap in Explant D was not identified during revision surgery. The relation of the prosthesis to the incus in its anterior and posterior part is easier to visualize because of a more favourable viewing angle and it remained tight in Explant D. In investigations of the mechanical aspects of this surgery (24), it has been found that complete circular contact is not a prerequisite for stable fixation of the prosthesis, even in long term follow-up after several months.

### **Reaction of the middle ear mucosa to the prosthesis**

The prosthesis hook was completely covered by mucosa in all explants. Also analysis by SEM showed that the prosthesis loop was covered by mucosa. Sim et al. (17) studied the influence on sound transmission of mucosa at the incus-prosthesis interface in 10 patients undergoing revision stapedotomy. They found only a minimal effect of ongrowing mucosa on sound transmission properties. A mucosal layer neither provides additional stability to compensate for inadequate crimping nor does it cause a loosening of the prosthesis' fixation on the incus. According to Lesinsky et al. (22), an extensive reaction of the middle ear mucosa with development of substantial scar tissue may cause a dislocation of the prosthesis. In our study, only minimal middle ear adhesions were found in two patients intraoperatively, which had no impact on fixation of the prosthesis but may have impaired its motion.

### **Alterations to the incudal bone**

A superficial, non circular erosion of the incudal bone was seen in Explant B on the anterior part and in Explant C on the posterior part. The posterior erosion in Explant

C was most likely caused by heat application of the laser during fixation because this is where the laser is usually aimed on the nitinol hook intraoperatively. Additionally, the round shape and the diameter correspond to the size of the laser beam and exceeded the width of the nitinol wire. The spot size of most lasers used in otology exceeds the diameter of the prosthesis wire used for the SMart piston, and coagulation of the tissue next to the loop is often observed during surgery. We have therefore started to apply a drop of saline solution on the prosthesis loop to prevent such superficial damage to the incus. The erosion in Explant B was likely not caused by laser application. It is on the anterior part of the incus, which is not reached by the laser, and it has a longish oval shape. It is therefore most likely a superficial erosion caused by the prosthesis. The erosion of the long process of the incus is a well-known complication after stapedotomy. However, the reason for this erosion remains a matter of debate. Three different hypotheses have been discussed:

(a) Overcrimping that causes traumatization of the bone (25), and a long term pressure or tension on the bone that impairs its metabolism. The width of the piston hook might be a critical factor for such erosion, according to Zahnert et al. (25). A slim hook results in larger forces per surface area compared to broad hooks. Therefore, a wide hook might be favorable as it decreases the pressure per area and reduces the collateral damage due to heat application during crimping. On the other hand, perpendicular axis might be lost (26). Schimanski et al. (27) describe a series of 5 Teflon-platin-pistons that completely migrated through the long process of the incus medially. Based on their SEM investigations, they state that the grooves on the surface of the prosthesis lead to adhesions of soft tissue that result in a medial traction due to scar formation. Therefore, they suggest a smooth surface and a conical shape of the piston in order to reduce the possibility of adhesions.

(b) Impaired blood supply can be the consequence of pressure or damage to the mucosa. However, according to Alberti et al. (28), the tip of the incus is supplied by bone marrow as well as anastomosis of the mucosa. Experiments in an animal model consider the blood supply of the bone marrow as being sufficient (28).

(c) A loose prosthesis can erode the bone due to permanent movement. Lesinski et al. (22) suppose that vibrations of the prosthesis lead to bony erosion of the incus. Besides suboptimal crimping, such situations may be induced or aggravated by foreign body reactions to the material of the piston that result in a local inflammatory reaction. Bone resorption and loosening of the prosthesis remain a matter of debate (27).

However, the erosions in Explant B and C had no influence on the prosthesis stability as judged during revision surgery, which was performed 40 (Explant B) and 16 month (Explant C) after the primary stapedotomy. Although superficial erosions were found in two Explants, there was no evidence of necrosis of the lenticular process. The follow-up of 6 to 40 month is relatively short. It remains unclear if a longer follow-up would result in a higher incidence of bone erosion.

#### Detection of nickel in the tissue around the prosthesis

Neither in energy dispersive x-ray analysis nor in atom absorption spectrometry was an increased concentration of nickel in comparison to the physiologic situation measurable.

Biocompatibility of nitinol has been investigated in several studies and seems to be mainly dependent on surface topography and handling during the process of prosthesis production (e.g., polishing, folding, sterilizing) (29, 30). The passive diffusion of nickel from the nitinol, measured by atom absorption spectrometry, reduces significantly over time, according to Wever et al. (31). After an initial release

there was no nickel release detected after 10 days because nitinol is stable and does not corrode in the presence of a TiO<sub>2</sub>-based surface layer. In vivo studies have revealed no allergic potential of nitinol such as irritations, systemic toxicity or sensitization (32). Two case reports, on the other hand, postulate a relationship between nitinol implants and systemic inflammatory reactions (33,34). A nickel allergy is not considered as a contraindication for nitinol stents (35). The total amount of nitinol in a stapes piston is much smaller compared to the nitinol stents used in cardiology. In addition, stapes prostheses are not surrounded by blood but by air in the middle ear space. This might result in faster development of a protective layer of titanium oxide and decrease the risk of allergic reaction.

The nickel concentration for wet weight in our explants was between 2.15 and 3.99 µg/g, whereas the concentration in the control group was between 1.86 and 4.04 µg/g. Large variability in the concentrations of nickel in human tissues has been reported in the literature, depending on the methods of measurement and sample processing and metabolic factors. Baranowska et al. (36) found a normal nickel content in human bones of 0.35 µg/g (range 0.14 to 2.58 µg/g), and according to the World Health Organization, the nickel threshold for drinking water is 70µg/l (37). Compared to these measurements, the concentration in our samples is in the upper range. However, the difference between our explants and the control group was within the same range, and the higher overall concentration likely resulted from using different equipment or measurement methods.

## **Conclusions**

Two limited superficial, but no circular, erosions of the incus were found in two explants. They did not alter prosthesis stability. All prostheses were covered by a mucosal layer that had no influence on stability. No signs of nickel deposits could be found on energy dispersive x-ray analysis or atom absorption spectrometry compared to a control group.

We consider nitinol stapes prostheses as being safe for implantation. Nevertheless, caution must be maintained in patients with a known allergy to nickel.

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## **Table and figure legend**

**Table 1**

Characteristics of the patients investigated.

	age	gender	side	time after primary surgery (month)
<i>Specimen</i>				
A	62	male	left	6
B	49	male	left	40
C	42	female	left	16
D	41	female	right	22

Table 2

Intraoperative findings of the 4 prostheses show a firm attachment of the prosthesis in all patients.

<i>INTRAOPERATIVE FINDING</i>	<i>Fixation of prosthesis on incus</i>	<i>Oval niche situation</i>	<i>Middle ear adhesions</i>	<i>Mobility of malleus</i>
<i>Specimen</i>				
<i>A</i>	good	correct prosthesis position	yes	restricted
<i>B</i>	good	correct prosthesis position	no	good
<i>C</i>	good	correct prosthesis position	no	good
<i>D</i>	good	Prosthesis fixation by scar tissue	yes	restricted

Table 3

Morphologic findings of the four prostheses showed a good fixation in the three explants available for investigation. A gap between prosthesis and incus was found in specimen D. Explant B was not available for morphologic investigation, see text.

<i>INTRAOPERATIVE FINDING</i>	<i>Fixation of prosthesis on incus</i>	<i>Gap between prosthesis and incus</i>	<i>Mucosal overgrowth</i>	<i>Limited erosions of incus</i>
<i>Specimen</i>				
<i>A</i>	good	no	complete	no
<i>B</i>	-	-	-	anterior
<i>C</i>	good	no	loop	posterior
<i>D</i>	good	lateral	complete	No

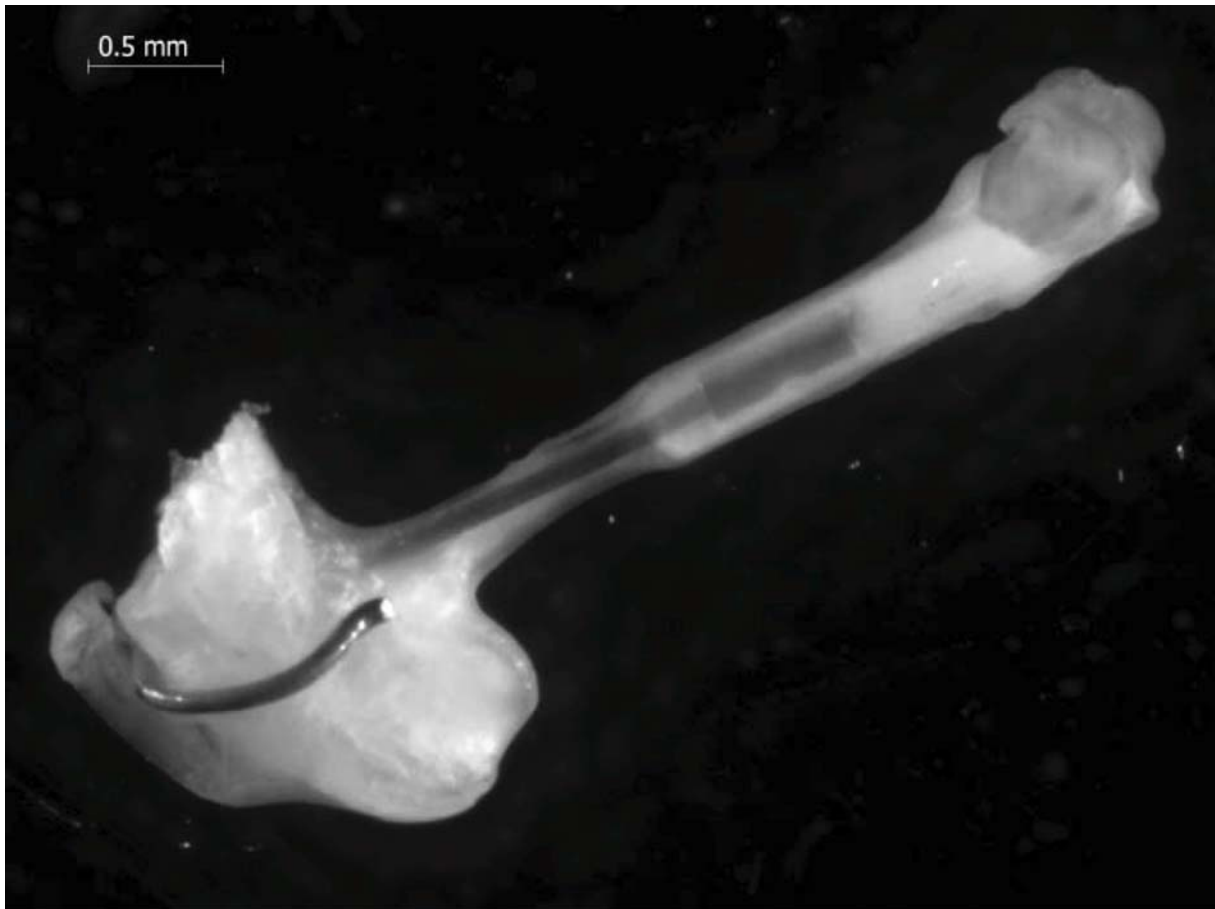
Table 4

Quantitative evaluation of the content of nickel in the incus using energy dispersive x-ray analysis. No increased values could be identified.

<i>Specimen</i>	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>
<i>NICKEL ANALYSIS</i>				
<i>Nickel content in bone (µg/g)</i>	2.78	3.19	2.15	3.99

Figure 1

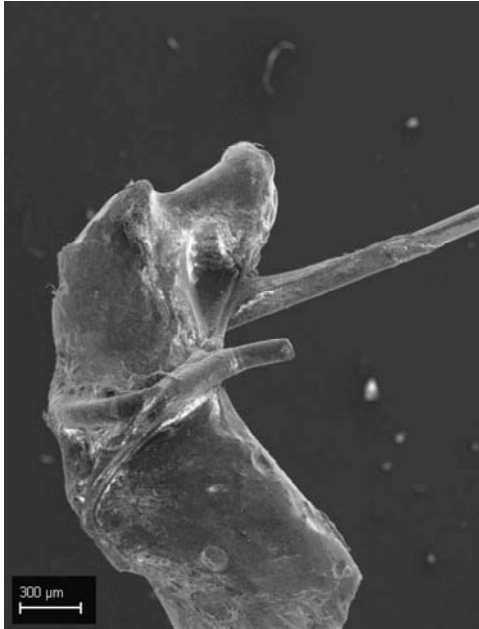
Macroscopy of Explant D with a gap between bone and prosthesis; incus in the lateral part.



## Figure 2

Left (a): SEM of Explant C. Firm fixation with circular attachment of the prosthesis on the bone (magnification 100x), Right (b): Explant D, gap between bone and the prosthesis in the lateral part (magnification 200x).

A)



B)

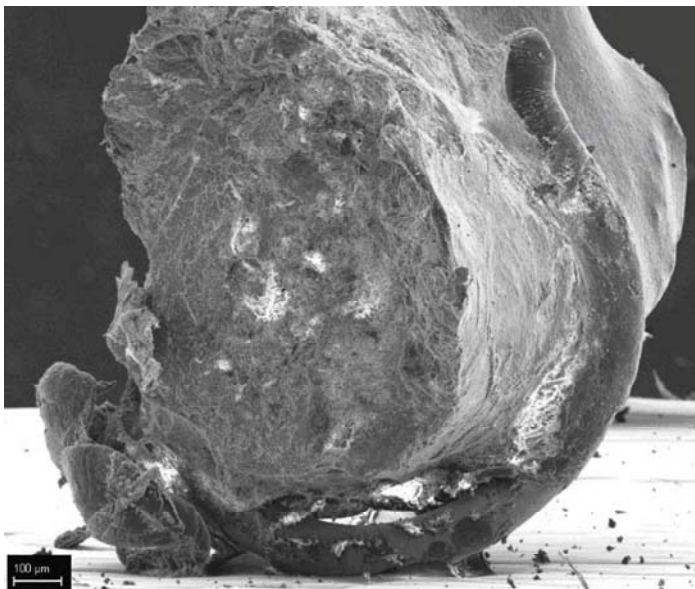
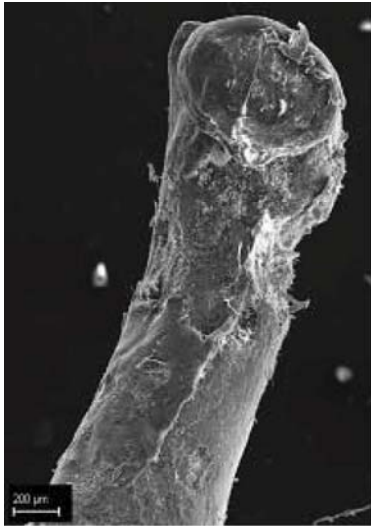


Figure 3

SEM of Explant C (left (a), magnification 100x) illustrating posterior erosion. The trabecules of the bone are visible in larger magnification (right (b), 2000x).

A)



B)

